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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,092	08/28/2006	**Gerd Wunderlich**	00415P0001WOUS	5931

30008 7590 05/24/2010

GUDRUN E. HUCKETT DRAUDT
SCHUBERTSTR. 15A
WUPPERTAL, 42289
GERMANY

EXAMINER	
RIDER, LANCE W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
05/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,092	WUNDERLICH ET AL.	
	Examiner	Art Unit	
	LANCE RIDER	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-31* is/are pending in the application.

4a) Of the above claim(s) *16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/11/2006 and 09/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 16-31 are currently pending, claims 16-23 have been withdrawn due to the election requirement filed on February 19th 2010.

Election/Restrictions

Applicant's election without traverse of Group II, claims 24-31 in the reply filed on March 18th 2010 is acknowledged.

Claims 16-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 18th 2010.

Information Disclosure Statement

The Information Disclosure Statements (IDS)s, filed by applicant on July 11th 2006 and September 20th 2006 have been considered by the examiner in the present case.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-29 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: Rhenium-188 and a base in the third container. Nowhere in the claims is any rhenium included in the kit.

Claims 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites that the kit contains "a quantity of a substance for increasing the pH value, the substance selected from..., present in solid form or in aqueous solution and generating in solution a pH value of pH 6.5 to 8.5". What does "a quantity of a substance" mean? Is it the amount of the compound that with yield a solution with a desired pH? If so, what is the initial solution and how much solution is there? The amount of compound necessary to alter the pH of a starting solution depends upon the initial pH, buffering capacity, and volume of the starting solution, none of which are defined. The claim also states that the substance can be in aqueous solution and generates a solution pH. Is the solution pH the pH of the aqueous solution, or the pH of some other solution which the aqueous solution is added to? For these reasons this claim is found indefinite. Claims 25-29 depend on this independent claim and do not rectify its indefinite nature.

Claim 28 recites the term "per administration to the patient". The claim is to a kit and not a method of treating a patient. What does "per administration to a patient"

mean? The examiner is interpreting this to mean that there is 0.02 mmol to 0.1 mmol of the tin-II salt present in the kit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-25, 27, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jia, W., et al., (J. of Radioanal. and Nuclear Cehmistry, 1995) provided in the IDS.

Jia discloses a container containing a 5 ml vial containing Tin(II) chloride, citric acid, and gentisic acid (2,5-dihydroxybenzoic acid). Jia also teaches a second vial containing 15 mg of HSA (human serum albumin) spheres. (See page 110, paragraph 2.) Jia discloses a third container containing sodium citrate from Aldrich Chemical Company. (See page 108, paragraph 4.) Jia also discloses protein microspheres of 10-15 um in diameter. (See page 112, paragraph 1.) These chemicals are all in separate containers as recited in the instant claims and meet the limitations of the kit claimed in instant claims 24-25, 27 and 29.

The particles of instant claims 30-31 are drawn to radioactive rhenium particles made by a process. "The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar

nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742,744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802,218 USPQ 289, 292 (Fed. Cir. 1983)

In the instant case the particles are made of polypeptide microspheres coated in ^{188}Re. The particles are also made by suspending particles of a protein at pH 3, adding rhenium, heating the solution, and re-suspended in isotonic saline ~pH 7.4. (See page 110, paragraph 2.) The instantly claimed particles have identical structural features to the instantly claimed particles and are made by a procedure similar procedure. The instantly claimed particles are therefore are anticipated by the particles of Jia.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jia, W., et al., (J. of Radioanal. and Nuclear Cehmistry, 1995) provided in the IDS in view of Sialerova, E., et al., (Applied Radiation, and Isotopes, 2003) provided in the IDS, and Rhodes U.S. Patent 5,078,985.

Jia teaches kits for making ^{188}Re labeled albumin microspheres.

Jia does not teach using sodium potassium tartrate as a buffer to bring the solution to physiological pH or using a tin-II-salt concentration of 0.02 mmol to 0.1 mmol.

Sialerova teaches methods for labeling protein microspheres with rhenium and the chemicals to label the microspheres (kits). Sialerova teaches using tartrate as a buffer to make rhenium labeled microspheres. Sialerova teaches the use of 200 to 800 ug/mL tin in the solution (0.0018 mmol to 0.007 mmol) and that the labeling of the microspheres is dependent upon the amount of tin in the solution. The range of tin used taught by Sialerova overlaps with the instantly claimed range of tin. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Sialerova teaches that at 800 ug/mL the microspheres are completely labeled when using low pH.

It would have been obvious to an artisan of ordinary skill in the art at the time of the invention to use accepted ranges of tin salts for rhenium labeling protein microspheres as taught by Sialerova in methods for rhenium labeling protein microspheres using tin salts. Sialerova teaches that using a concentration of 800 ug/mL tin can completely label the microspheres. Thus the skilled artisan would have been motivated to use the concentration of 800 ug/mL tin taught by Sialerova in the method of Jia in order to form completely labeled microspheres.

Jia and Sialerova do not teach the use of sodium potassium tartrate as the tartrate buffer used in labeling protein microspheres with rhenium. Jia and Sialerova teach methods to label protein microspheres with rhenium using tartrate buffer. They do not disclose the counterions in the tartate buffer.

Rhodes teaches methods and kits for radiolabeling protein microspheres with rhenium. Rhodes teaches using sodium potassium tartrate as a buffer in these kits. Rhodes teaches solid sodium potassium tartrate and solutions of sodium potassium tartrate. (See column 5, line 59.)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use a commonly used buffer sodium potassium tartrate, taught by Rhodes, as the source of the tatrate buffer in the methods of Jia and Sialerova. This is merely the use of an art recognized buffer used in rhenium labeling of protein microspheres in a method for rhenium labeling of microspheres which calls for a tartrate buffer. The skilled artisan would have predicted that this combination would function as both procedures use tartrate as a buffer in making the protein microspheres and Rhodes teaches that sodium potassium tartrate functions in such methods as a suitable buffer.

Conclusion

No claims are currently allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/
Examiner, Art Unit 1618

/Eric E Silverman/
Primary Examiner, Art Unit 1618